Pergamon

Tetrahedron Letters 43 (2002) 3841–3844

TETRAHEDRON
LETTERS

Regioselectivity and selective enhancement of carbon dioxide fixation of 2-substituted aziridines to 2-oxazolidinones under supercritical conditions

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Received 6 February 2002; revised 4 April 2002; accepted 5 April 2002

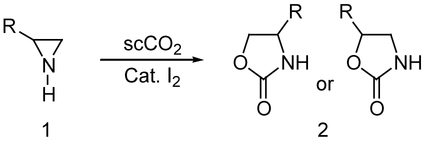
Abstract—Under supercritical CO_2 conditions, regioselectivity in the carbon dioxide fixation of 2-substituted aziridines to 2-oxazolidinones was observed with good yields around 75%. Furthermore, when propylene imine was used in the place of aziridine, the yield was significantly and selectively increased around the critical pressure, and the maximum yield was obtained at 11.8 MPa. The turnover frequency (TOF) at this pressure is 2.1 times greater than that of a hitherto reported TOF which was obtained in ethanol at 6.9 MPa. © 2002 Published by Elsevier Science Ltd.

From the standpoint of the protection of the environment, development of environmentally benign processes using chemical fixation of carbon dioxide, one of the greenhouse-effect gases, has been drawing much interest in industrial chemistry and biotechnology, because there are numerous possibilities that carbon dioxide can be used as a safe and cheap C1 component to produce useful organic compounds.

The chemical fixation of carbon dioxide from aziridine into 2-oxazolidinones has been reported,[1,2] since 2-oxazolidiones are widely available in organic synthesis as chiral auxiliaries or useful building blocks for a variety of bioactive compounds.[3–5] However, these reactions have been taken place using CO_2 gas under disadvantageous conditions from the viewpoints of an industrial and environmentally-friendly production process, e.g. at reaction times longer than 21 h in organic solvents,[1a,1b] or in the presence of organoantimony catalysts[1c,1d] or via flash vacuum pyrolysis at 600°C in the presence of ethyl chlorocarbonate,[2a] or by electrochemical procedure in the presence of nickel complex catalyst,[2b] because of the low reactivity of CO_2 (Scheme 1).

Supercritical CO_2 ($scCO_2$) has been attractive not only as a conventional reaction medium but also as a good substrate,[6] and organic reactions under $scCO_2$ conditions are expected to be promoted even at low temperatures due to enhanced diffusivity and disappearance of the gas–liquid phase boundary peculiar to the supercritical state.[7] Recently, some interesting chemical fixations of CO_2 have been carried out under supercritical conditions, and successfully produced to carbamates or carbonates in good yields.[8,9] In this work, we found that under $scCO_2$ conditions, carbon dioxide fixation by aziridine was regiospecific, and only the formation of 4-methyl-2-oxazolidinone from 2-methyl aziridine in the presence of iodine was significantly enhanced even at a lower temperature of 40°C.

The reaction of aziridines **1** with carbon dioxide in the presence of iodine as a Lewis acid catalyst was conducted in batchwise operation under various conditions as shown in Table 1.[10] Six-hour reactions under supercritical conditions produced 2-oxazolidinones from both propylene imine **1a** and 2-phenyl aziridine **1b** (runs 5, 12). In the case of **1a**, only 4-methyl-2-oxazolidione **2a** was obtained,[1,11,12] whereas 5-phenyl-2-oxa-



Scheme 1.

Keywords: aziridine; oxazolidinone; supercritical carbon dioxide; carbon dioxide fixation.

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0040-4039/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0040-4039(02)00676-7

Table 1. Reaction of propylene imine **1a** and 2-phenyl aziridine **1b** with carbon dioxide in the presence of iodine under various pressures[a]

Run	Substrate	Pressure (MPa)	Temperature (°C)	Reaction time (h)	Yield of 2-oxazolidinone (%)	TOF[f] (h^{-1})
1	Propylene imine **1a**	2.1	40	2	17[b]	2.1
2		8.0	40	2	21[b]	2.6
3		10.0	40	2	25[b]	3.3
4		11.8	40	2	46[b]	7.2
5		11.8	40	6	72[b,c]	7.2
6		15.7	40	2	37[b]	5.2
7		6.9	80	21	44[d]	3.3
8	2-Phenyl aziridine **1b**	2.1	40	2	76[e]	16.2
9		8.0	40	2	50[e]	7.8
10		10.0	40	2	38[e]	5.5
11		11.8	40	2	33[e]	4.6
12		10.0	40	6	76[e]	5.5

[a] Cat.: I_2 0.1 mmol; co-solvent: EtOH 1.0 mL (2.0 vol.%). MeOH and MeCN are also available as co-solvents.

[b] Compound **2a** was formed.

[c] 2,5-Dimethyl piperazine was obtained in a 28% yield.

[d] Ref. 1a. The solvent was EtOH.

[e] Compound **2b** was formed.

[f] The rate constants were obtained as the pseudo first-order rate constant.

zolidinone **2b** was formed without regioisomers when **1b** was used.[13] These regiospecific results are similar to those of the reaction of aziridines with hydrochloric acid[14] or the reaction of aziridines in the presence of organoantimony halides.[1d] We thus propose the following two plausible reaction mechanisms of aziridines **1a**, **1b** (Scheme 2) to transform into 2-oxazolidinones **2a**, **2b**. In the case of the formation of **2a**, **1a** reacts with carbon dioxide directly at the nitrogen atom to form carbamic acid **3** which attacks the β-carbon atom of another aziridine molecule **1a′** to afford **2a** (Path A). On the other hand, the formation of **2b** could be ascribed to the generation of 1,3-dipole **5**, which was proposed by Mann et al.[15] Then, **5** would react with $scCO_2$ to form **2b** through Path B. In the reaction of **1a**, an increase in the yield of **2a** with increasing pressure was observed in Table 1 (runs 1–4). Furthermore, turnover frequency (TOF) at 11.8 MPa (run 4) is 3.4 times larger than that at 2.1 MPa (run 1), and is a further 2.1 times larger than a previously reported TOF in ethanol at 6.9 MPa and 80°C (run 7).[1a] This enhancement of the yield would be due to the disappearance of gas–liquid phase boundary in $scCO_2$.

Fig. 1 shows a pressure dependence of the yield of **2a** (reaction temperature: 40°C; reaction time: 2 h). One can see an interesting pressure dependence, in which the yield increases outstandingly with increasing pressure,

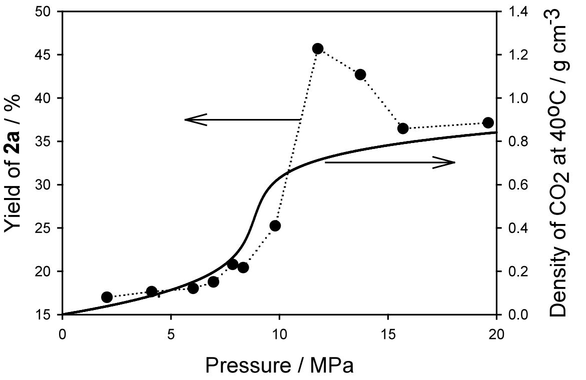
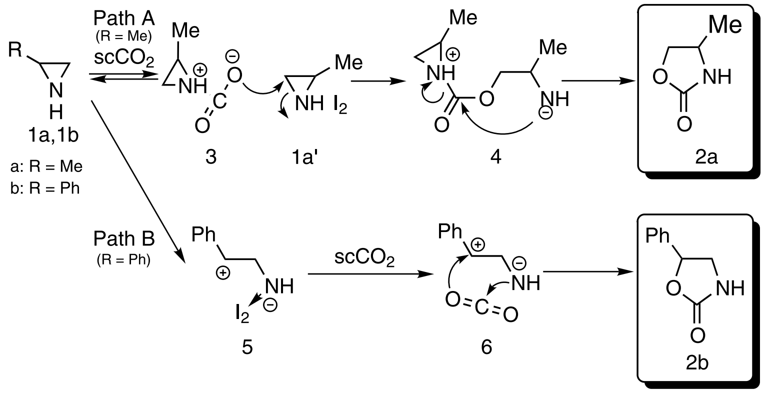


Figure 1. Pressure dependence of the yield of 4-methyl-2-oxazolidinone in the presence of iodine, and CO_2 density at 40°C under various pressures, which was obtained from NIST Standard Reference Database.



Scheme 2. Plausible reaction mechanism to form 4-methyl-2-oxazolidinone **2a** and 5-phenyl-2-oxazolidinone **2b**.

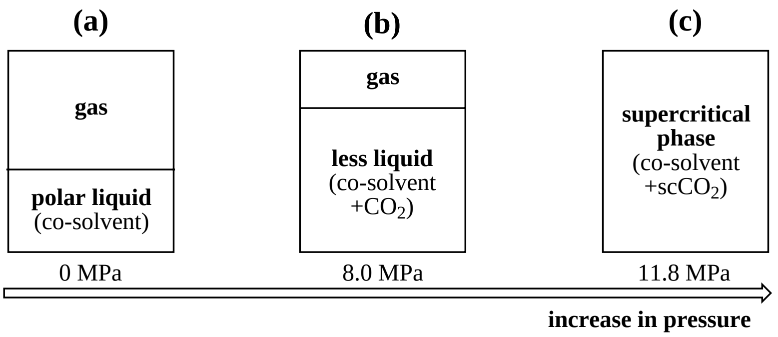


Figure 2. A schematic diagram of the phase behavior of the co-solvent/CO_2 mixture in a reaction vessel at 40°C.

reaching a maximum yield at the near-critical pressure of 11.8 MPa. In order to explain the significant increase in yield in the near critical region, CO_2 density was also shown in Fig. 1.[9] It can be found that the increase in CO_2 density with pressure shows relatively good agreement with the increase in yield of **2a** (Fig. 1). In the case of the reaction of **2a**, increasing the mole fraction of CO_2 by increasing density of CO_2 under constant volume can contribute to a shift in the equilibrium (Path A in Scheme 2) in favor of the generation of **3**, then leading to an increase in the yield of **2a** by the irreversibly nucleophilic attack of **3** to **1a**′ in CO_2. At the near critical pressure of 11.8 MPa, we can see higher yields than those expected from the relationship between the yields and the CO_2 density, which cannot be understood by only an increase in the formation of **3**. To clarify the unusual increase in yield, visual observation was carried out using a high-pressure view cell. Above 10.2 MPa, gas–liquid binary phase had disappeared to form a homogeneous fluid phase which is regarded as the supercritical state. It is likely that a significant increase in local concentration[16,17] of reactant **1a** around **3** would be very large, around 11.8 MPa, resulting in the outstanding increase in yield as seen in Fig. 1.

In Table 1, a decrease in the yield of **2b** with increasing pressure was further observed (runs 8–11).[18] Since the reaction took place in the liquid or supercritical phase, this decrease could be explained by the variation of CO_2 content in each phase which occurred during the increase in pressure.[19] When the CO_2 is introduced as shown in Fig. 2, the liquid phase changes from the polar phase containing only the co-solvent to a less polar one made up of CO_2 and the co-solvent (a to b) and to a further less polar solvent (b to c), because the content of only non-polar CO_2 in the liquid phase is increased with increasing pressure.[19] In the less polar phase such as b and c, the formation of 1,3-dipole **5** with a transient benzylic carbocation and a negative charged nitrogen would be prevented, because the ionization reaction which proceeds as S_N1 is known to be decelerated.[1d,20] Thus, the carbon dioxide fixation through path B would be more unfavorable in $scCO_2$. Consequently, under the supercritical conditions the reaction of CO_2 with **1a** would be more favored than that with **1b**.

In conclusion, we have demonstrated that carbon dioxide fixation by 2-methyl aziridine in the presence of iodine was effectively converted into 4-methyl-2-oxazolidinone without regioisomers under supercritical conditions, and the maximum yield was obtained at the near critical pressure of 11.8 MPa.

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10. The typical experimental procedure is as follows: propylene imine (3.0 mmol), iodine (0.1 mmol) and acetonitrile (1.0 mL) were charged into a 50 cm^3 reactor at 40°C and CO_2 was introduced into the reactor. In the case of the $scCO_2$, liquid CO_2 was subsequently charged into the reactor using a high-pressure liquid pump and com-

pressed to the desired pressure. Pressure control was achieved by a back-pressure regulator. The reactions in both the CO_2 and $scCO_2$ were started by stirring the mixture, continued for 2 h. After reaction, the reactor was cooled to 0°C with ice and the pressure was released slowly. 2-Oxazolidinone was purified from the crude products by distillation (the isolated yield was 67% at 11.8 MPa) and was analyzed by NMR. The yields of the product were determined by GC–MS using a tridecane as an internal standard.

11. 4-Methyl-2-oxazolidinone (racemic): ^1H NMR (500 MHz, $CDCl_3$) δ 6.67 (^1H, br s, NH), 4.95 (1H, dd, $J=7.8$ Hz, 5-CH2), 4.00 (1H, ddq, $J=7.7$ Hz, $J=6.0$ Hz, $J=6.0$ Hz, 4-CH-Me), 3.92 (1H, dd, $J=8.1$ Hz, $J=8.0$ Hz, 5-CH_2), 1.28 (3H, d, $J=6.0$ Hz, 4-CH_3).
12. The reaction of **1a** with $scCO_2$ under non-co-solvent condition was carried out and the yields of **2a** were 37% at 2.0 MPa, 66% at 11.8 MPa and 35% at 19.5 MPa, respectively. The maximum yield was also obtained at near critical pressure of 11.8 MPa.
13. 5-Phenyl-2-oxazolidinone (racemic): ^1H NMR (500 MHz, $CDCl_3$) δ 7.47–7.39 (5H, m, ph), 6.50 (1H, br s, NH), 5.60 (1H, dd, $J=8.0$ Hz, 5-CH-Ph), 4.03 (1H, dd, $J=8.5$ Hz, 4-CH_2), 3.59 (1H, dd, $J=8.5$ Hz, 4-CH_2).
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